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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/315,116	05/19/1999	DOUGLAS ANTELMAN	16930-0010-2	6044

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EXAMINER
KAUSHAL, SUMESH

ART UNIT	PAPER NUMBER
1636	17

DATE MAILED: 04/17/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/315,116	ANTELMAN ET AL.	
	Examiner	Art Unit	
	Sumesh Kaushal Ph.D.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 February 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16-37* is/are pending in the application.

4a) Of the above claim(s) *31-36* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *16-30 and 37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicant's response filed on 02/06/03 has been acknowledged.

Claims 16-37 are pending and are examined in this office action.

This application contains claims 31-36 drawn to an invention nonelected with traverse in Paper No. 12. A complete reply to the final rejection must include cancelation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claims 16-30 and 37 are examined in this office action.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The references cited herein are of record in a prior Office action.

► *Applicants are advised to follow Amendment Practice under revised 37 CFR §1.121 (http://www.uspto.gov/web/offices/pac/dapp/opla/preognotice/revamdtprac.htm). Each amendment document that includes a change to an existing claim, or submission of a new claim,* ***must include a complete listing of all claims*** *in the application. After each claim number, the status must be indicated in a parenthetical expression, and the text of each claim under examination (with markings to show current changes) must be presented. The listing will serve to replace all prior versions of the claims in the application.*

Claim Rejections - 35 USC § 112

Claims 16-30 and 37 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled

in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention for the same reasons of record as set forth in the office action mailed on 07/31/02.

Nature Of Invention:

The invention as claimed relates to a method of treating hyperproliferative disorder in a patient via a method of gene therapy.

Breadth Of Claims And Guidance Provided By The Inventor:

The claimed invention is directed to a method for treatment of a hyperproliferative disorder in a patient comprising administering to a patient a therapeutically effective dose of a nucleic acid encoding a fusion polypeptide or a fusion polypeptide that comprises a DNA binding domain of a transcription factor, or E2F, or amino acid fragment of SEQ ID NO: 1 or 4. At best the specification demonstrated cell cycle arrest and growth suppression of 5687 bladder cells in-vitro by RB and RB-E2F fusion proteins (specification page 24, Table 1.2). The only guidance that is related with a disease model is the inhibition of restenosis using a rat model with balloon induced injury (specification, page 29, line 15.28), which does not correlate with the treatment of a cancer especially bladder cancer.

State Of Art And Predictability:

The state of the art at the time of filing teaches that cancer is the most challenging hyperprolerative disease, which is the result of the accumulation of multiple abnormalities that elicits multi step development. Various tumor suppressor genes have been recognize to be related with certain type of carcinomas (Cooper, Oncogenes, Jones and Bartlett Publishers, 1990). There is evidence that environmental exposure also related with cancer formation (Heather, et al. J. Cell. Biochem. 25S:15.22, 1996). Like most of other malignancies the generation of bladder cancer is caused by the accumulation of numerous molecular changes. The expression of oncogenes (ras, erbB-2 and EGF receptor), tumor-suppressor genes (Rb, p53), cell-cycle genes (p15, p16) and DNA-repair genes are altered mostly by mutation or chromosomal aberration (Brandau et al. Eur. Urol. 39:491.497, 2001). Besides pRb, alteration in p53 expression is also known to occur in early state bladder carcinoma (Reznikoff et al). Furthermore corrective cancer gene therapy requires correction of genetic defect in all the cancer cells, since malignant clones can expand and metastasized. Correction of single genetic defect in a multi step process of genetic hits may not be sufficient once the cancer has produced a fully invasive and metastasized

clones (Carducci et al. Cancer Treat. Res., 88:219.84, 1996). Furthermore the gene therapy is considered highly experimental area of research at this time, and both researchers and the public agree that demonstrable progress to date has fallen short of initial expectations. It has been difficult to predict the efficiency and out come of transduced therapeutic genes because various factors govern the expression and/or therapeutic potential of transduced genes in vivo. In addition, in vitro gene transfer studies are not predictive of in vivo gene therapy because gene transfer frequency is much higher in-vitro models where most of cells are under going rapid cell division, which is quite not the case in vivo environment. In addition, besides the limitations in gene transfer the problem to selectively target cells in vivo is still one of the most difficult obstacle to overcome. The viral particles binds to many cells they encounter in vivo and therefor would be diluted out before reaching their targets (Anderson WF, Nature 392:25-30, 1998). Although, the gene therapy holds much promise to come, the success will only be achieved through continued rigorous research on the most fundamental mechanisms that contribute to a genetic disease along with the pathogenesis of the disease, gene delivery and gene expression in animals

Response to arguments

The applicant argues that Cooper clearly teaches that introduction of a functional normal Rb gene reverses the tumorigenicity of the retinoblastoma cell lines in which endogenous gene has been deleted (response page 3-4). The applicant argues that even though Chellappan teaches E2F exits in complexes with different cellular proteins the purpose of present invention is to provide E2F DNA binding portion in order to tether the fusion polypeptide of the DNA (response, page 4 para.2). The applicant argues that the composition and method of the present invention are broadly applicable to number of different target cells for number of different hyperproliferative disorders and there is ample teaching in the specification to exercise the invention without undue experimentation (response, page 4 para.3). The applicant argues that under lying conclusion that gene therapy is unpredictable to achieve useful results is incorrect (response, page 6 para.1-2). The applicant further argues that an applicant is not required to solve all technical problems in this field so long as he has taught how to practice the claimed invention without undue efforts (response, page 6 para.3).

However, this is found NOT persuasive because applicant's argument alone cannot take place of evidence lacking in the record (see In re Scarbrough 182 USPQ, (CCPA) 1979). The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). The invention as claimed is drawn to a method of treating any and all hypeproliferative disorders wherein in the hypeproliferative disorder is not limited to a bladder cancer. At best the applicant's disclosure only teaches suppression of cell growth in RBneg and 5637 bladder cell lines in vitro, wherein the plasmid encoding the fusion polypeptide (as claimed) has been transfected by using lipofectin reagent (spec. page 24). Considering the unpredictability in the state of cancer art and the art of gene therapy, the specification as filed fails to provide a single working example that teaches the treatment of any and all hypeproliferative disorder by administering nucleic acid encoding the fusion polypeptide (as claimed). The specification even fails to disclose how the nucleic acid which encodes the polypeptide (as claimed) are administered to a patient to target cancer cells in vivo. Furthermore considering the applicant's disclosure it is even unclear how one skill in the art would target cancer cells that has been metastasized in vivo. ***In instant case gene based caner therapies are not routine in the art and without sufficient guidance to a specific therapeutic gene the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.*** See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). It is noted that the unpredictability of a particular area may alone provide reasonable doubt as to the accuracy of the broad statement made in support of enablement of claims. See Ex parte Singh, 17 USPQ2d 1714 (BPAI 1991).

Furthermore, it is noted that patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable (*See Brenner v. Manson , 383 U.S. 519, 536, 148 USPQ 689, 696 (1966), Stating, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion"*) Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention. Therefore, considering the unpredictability in the treatment of any hypeproliferative

disorder and state of gene based therapies one skill in the art would have to engage in excessive and undue amount of experimentation to exercise the invention as claimed.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal Ph.D. whose telephone number is 703-305-6838. The examiner can normally be reached on Mon-Fri. from 9AM-5PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yucel Irem Ph.D. can be reached on 703-305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-8724 for After Final communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

S. Kaushal
PATENT EXAMINER

JEFFREY FREDMAN
PRIMARY EXAMINER